Remarks

Claim Rejections 35 USC § 112

The Examiner has rejected claims 1-6, 8 and 11-16 under 35 USC § 112, first paragraph as failing to comply with the written description requirement. Specifically, referring to the limitation of independent Claim 1 reading "non-liposome multilamellar crystal non-polar phosphatidylcholine" (sic, page 3, lines 1-2 of Office Action). As noted in Applicants' Response to Office Action filed 31 October 2007, support for the amended claims is provided in the application at page 5, ¶ [0013].

In the Office Action at page 3, lines 6-7 it states "The Examiner cannot envision how phosphatidylcholine could be non-polar because it is a charged molecule". The applicants believe that this is a misunderstanding resulting from a misreading of Claim 1 which actually reads "non-liposome multilamellar liquid crystal phosphatidylcholine non-polar carrier". Thus it indicates that the carrier superstructure as a whole is non-polar, not that the phosphatidylcholine component of the carrier is non-polar. While it is true that individual molecules of phosphatidylcholine might be polar due to charge considerations, aggregates of phosphatidylcholine molecules may, as a whole, be non-polar in a manner similar to the way that cell membranes are non-polar, although the individual molecules which make up such membranes may be polar.

Liposomes have two chief characteristics being that they have a) a surrounding lipid membrane and b) an aqueous center compartment. Such structures are well known to persons of ordinary skill in the art. The term "non-liposome" is used to communicate to those skilled in the art that the carrier described in the application is not a liposome.

The Examiner has also rejected claims 1-6, 8 and 11-16 under 35 USC § 112 second paragraph. This rejection is based on the incorrect reading of claim 1 which recites a "non-polar carrier". As previously pointed out, it is possible, and there are many examples of non-polar structures built out of polar and even charged molecules. The previously cited example of cell membranes is just such a structure. Their overall non-

polar nature is demonstrated by the inability of polar ions such as sodium or potassium to freely pass through them, requiring special transport pumps to move such polar ions through the membranes, whereas lipophilic drugs pass through with much greater ease. It is respectfully submitted that claims 1-6, 8 and 11-16 are described in this specification and are definite. The rejections under 35 U.S. § 112 should be withdrawn.

Claim rejections 35 USC § 103(a)

Claims 1-6, 8 and 11-16 have been rejected as being obvious under 103(a), and therefore unpatentable, over Amselen et al (US 5662932) or Lynch (US 2002/0153509) in view of Hansen (US 4614730) and Patel (US6294192), and with respect to claims 2-6, 8, 15 and 16, Chaiyawat (U.S. 6538061) and Brieva (U.S. 5985298). This rejection is respectfully traversed.

Amselen is cited as teaching a method of preparing a 'nanoemulsion" comprising preparing a mixture comprising phosphoplipid and triglyceride. These nanoemulsions are described by Amselen as having features "which are intermediate between liposomes and oil-in-water emulsions." (Column 2 lines 37-38) The "emulsome" particles contain a hydrophobic core (the triglyceride), as in standard oil-in water emulsions, which is surrounded layers of phospholipid molecules, as in liposomes. Simply put, Amselen claims liposomes which have a lipid filled center rather than an aqueous center as in traditional liposomes. This hydrophobic triglyceride center can therefore contain hydrophobic drug molecules. The triglyceride, therefore is an essential component of the carrier which Amselen describes.

In contrast, the carrier of the present invention requires no such triglyceride component. The polyglycol used in the preparation of the carrier of the present invention is the antithesis of the hydrophobic triglyceride used in Amselen. It is added in order to help solubilize the insulin which has limited solubility in lipid environments and to stabilize it at room temperature.

The Examiner asserts that "Amselen et al. teach that rigid bilayer envelopes are expected thus reading on multilamellar." The applicants respectfully disagree with this

interpretation. Phospholipids will naturally associate in bilayer structures and each bilayer structure constitutes a single layer, which is two molecules thick. The term bilayer is not synonymous with multilamellar.

Amselen does teach that nonnatural surfactants may be added but indicates that they comprise "most preferably less than 0.1%. A significant advantage of emulsomes is that they may be prepared as a stable emulsion in the essential absence of nonnatural surfactants." (column 8, lines 2-5). Amselen thus teaches that these surfactants are not required and, if used, should be kept to a minimum amount.

In contrast, the polyethylene glycols used in the present invention comprise up to 55% of the carrier and are thus an essential part of the carrier of the present invention.

Amselen et al. teach the preparation of a lipid-filled liposome. The combination of this lipid-filled liposome with either the insulin solutions of Hansen, or the polyethylene glycols of Patel would not allow one to arrive at the carrier described within the present invention. The claims of the present invention are therefore patentable over Amselen in view of Hansen and/or Patel. This is similarly true of the teaching of Amselen in view of Hansen and Patel in view of the silicone components of Chaiyawat and Brieva.

Lynch et al teach of a "cubic liquid crystalline phase precursor comprising (A) an ambiphile capable of forming a cubic liquid crystalline phase, (B) an optional solvent and (C) an additive selected from the group consisting of an anchor, a tether and combinations thereof such that 1.0=A+B+C and 1>A>0, 1>B>0 and 1>C>0. (i.e each of A, B and C must be present in some quantity). The "tether" C is identified as having a charged end and a lipid tail in [0055] to [0059]. The carrier of the present invention requires no similar ingredient as that described as the "tether" in Lynch, which requires its presence. Since no comparable C component is present in the carrier of the present invention the claims of the present invention are therefore patentable over Lynch in view of Hansen and/or Patel. This is similarly true of the teaching ofLynch in view of Hansen and Patel in view of the silicone components of Chaiyawat and Brieva.

The present invention provides for a method of formulating an insulin composition within a phosphatidylcholine carrier, wherein said insulin is stabilized at room temperature. Neither the disclosed invention nor its benefits are disclosed or suggested by the combination of references. It is submitted that the presently claimed invention is patentable over Lynch et al. and over Amselem et al. in view of Patel and/or Hansen and Chaiyawat and/or Brieva, and issuance of a Notice of Allowance is respectfully requested.

Respectfully submitted,

May 7, 2008

/Stephen P. McNamara/

Stephen P. McNamara, Registration No. 32,745
Attorney for Applicants
ST. ONGE STEWARD JOHNSTON & REENS LLC
986 Bedford Street
Stamford, CT 06905-5619
Tel. 203 324-6155